REMARKS

Applicants have discovered that there are inadvertent errors in the Specification and Sequence Listing and have corrected these errors at describeded below.

It is respectfully submitted that the present amendment presents no new issues or new matter.

I. Specification

Applicants have discovered that pages 8-10 of the specification contain inadvertent typographical errors. SEQ ID NO: 1, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, and SEQ ID NO: 11, should be SEQ ID NO: 5, SEQ ID NO: 21, SEQ ID NO: 17, SEQ ID NO: 23, and SEQ ID NO: 13. Support for these corrections is found in Example 6 (SEQ ID NO: 1 to SEQ ID NO: 5), Example 11 (SEQ ID NO: 5 to SEQ ID NO: 21), Example 10 (SEQ ID NO: 7 to SEQ ID NO: 17), Example 12 (SEQ ID NO: 9 to SEQ ID NO: 23), and Example 9 (SEQ ID NO: 11 to SEQ ID NO: 13). Moreover, the two paragraphs relating to SEQ ID NO: 3 have been deleted since the nucleotide sequence of the *asa* gene is not SEQ ID NO: 3. SEQ ID NO: 3 is a primer described in Example 4. The *asa* gene is described in Example 8 with reference to U.S. Patent No. 5,252,726.

Pages 8-10 of the Specification have been amended to correct these inadvertent typographical errors. A marked-up version of pages 8-10 is submitted under 37 CFR 1.125.

Applicants respectfully request that the marked-up version be entered.

II. New Sequence Listing

Applicants have also discovered that SEQ ID NO: 14 is incorrect. SEQ ID NO: 14 is the deduced amino acid sequence of SEQ ID NO: 13. In the preparation of the Sequence Listings, Applicants inadvertently inserted SEQ ID NO: 30 in place of SEQ ID NO: 14 so SEQ ID NO: 30 appears twice in the Sequence Listings as SEQ ID NO: 14 and SEQ ID NO: 30. Applicants have corrected SEQ ID NO: 14 so it is the deduced amino acid sequence of SEQ ID NO: 13. The deduced amino acid sequence is inherent to the DNA sequence of SEQ ID NO: 13

Applicants enclose a paper copy and a computer readable form of a new Sequence Listing containing the correct SEQ ID NO: 12, as described above. The content of the paper copy and of the computer readable form is the same. This submission contains no new matter.

Please delete the previously submitted Sequence Listing and insert the attached Sequence Listing (pages 1-37) at the end of the specification.

III. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: August 17, 2007

Robert L. Starnes, Ph.D.
Reg. No. 41,324
Novozymes, Inc.
1445 Drew Avenue
Davis, CA 95618
(530) 757-4715

The *Aspergillus niger* mutant strains may also be constructed by established anti-sense techniques using a nucleotide sequence complementary to the nucleotide sequence of the gene (Parish and Stoker, 1997, *FEMS Microbiology Letters* 154: 151-157). More specifically, expression of the gene by an *Aspergillus niger* strain may be reduced or eliminated by introducing a nucleotide sequence complementary to the nucleotide sequence of the gene, which may be transcribed in the strain and is capable of hybridizing to the mRNA produced in the strain. Under conditions allowing the complementary anti-sense nucleotide sequence to hybridize to the mRNA, the amount of protein translated is thus reduced or eliminated.

The *Aspergillus niger* mutant strains may be further constructed by random or specific mutagenesis using methods well known in the art, including, but not limited to, chemical mutagenesis (see, for example, Hopwood, *The Isolation of Mutants* in *Methods in Microbiology* (J.R. Norris and D.W. Ribbons, eds.) pp 363-433, Academic Press, New York, 1970) and transposition (see, for example, Youngman *et al.*, 1983, *Proc. Natl. Acad. Sci. USA* 80: 2305-2309). Modification of the gene may be performed by subjecting the parent strain to mutagenesis and screening for mutant strains in which expression of the gene has been reduced or eliminated. The mutagenesis, which may be specific or random, may be performed, for example, by use of a suitable physical or chemical mutagenizing agent, use of a suitable oligonucleotide, or subjecting the DNA sequence to PCR generated mutagenesis. Furthermore, the mutagenesis may be performed by use of any combination of these mutagenizing methods.

Examples of a physical or chemical mutagenizing agent suitable for the present purpose include ultraviolet (UV) irradiation, hydroxylamine, N-methyl-N'-nitro-N-nitrosoguanidine (MNNG), N-methyl-N'-nitrosogaunidine (NTG) O-methyl hydroxylamine, nitrous acid, ethyl methane sulphonate (EMS), sodium bisulphite, formic acid, and nucleotide analogues. When such agents are used, the mutagenesis is typically performed by incubating the parent strain to be mutagenized in the presence of the mutagenizing agent of choice under suitable conditions, and selecting for mutants exhibiting reduced or no expression of a gene.

In a preferred aspect, *glaA* comprises a nucleotide sequence having at least 70%, preferably at least 75%, more preferably at least 80%, even more preferably at least 85%, most preferably at least 90%, and even most preferably at least 95% identity to ~~SEQ ID NO: 1~~ SEQ ID NO: 5. In a most preferred aspect, *glaA* comprises the nucleotide sequence of ~~SEQ ID NO: 1~~ SEQ ID NO: 5. In another most preferred aspect, *glaA* consists of the nucleotide sequence of ~~SEQ ID NO: 1~~ SEQ ID NO: 5.

In another preferred aspect, *glaA* comprises a nucleotide sequence which hybridizes under very low stringency conditions, preferably low stringency conditions, more preferably medium stringency conditions, more preferably medium-high stringency conditions, even more

preferably high stringency conditions, and most preferably very high stringency conditions with ~~SEQ ID NO: 1~~ SEQ ID NO: 5.

~~In a preferred aspect, *asa* comprises a nucleotide sequence having at least 70%, preferably at least 75%, more preferably at least 80%, even more preferably at least 85%, most preferably at least 90%, and even most preferably at least 95% identity to SEQ ID NO: 3. In a most preferred aspect, *asa* comprises the nucleotide sequence of SEQ ID NO: 3. In another most preferred aspect, *asa* consists of the nucleotide sequence of SEQ ID NO: 3.~~

~~In another preferred aspect, *asa* comprises a nucleotide sequence which hybridizes under very low stringency conditions, preferably low stringency conditions, more preferably medium stringency conditions, more preferably medium-high stringency conditions, even more preferably high stringency conditions, and most preferably very high stringency conditions with SEQ ID NO: 3.~~

In a preferred aspect, *amyA* comprises a nucleotide sequence having at least 70%, preferably at least 75%, more preferably at least 80%, even more preferably at least 85%, most preferably at least 90%, and even most preferably at least 95% identity to ~~SEQ ID NO: 5~~ SEQ ID NO: 21. In a most preferred aspect, *amyA* comprises the nucleotide sequence of ~~SEQ ID NO: 5~~ SEQ ID NO: 21. In another most preferred aspect, *amyA* consists of the nucleotide sequence of ~~SEQ ID NO: 5~~ SEQ ID NO: 21.

In another preferred aspect, *amyA* comprises a nucleotide sequence which hybridizes under very low stringency conditions, preferably low stringency conditions, more preferably medium stringency conditions, more preferably medium-high stringency conditions, even more preferably high stringency conditions, and most preferably very high stringency conditions with ~~SEQ ID NO: 5~~ SEQ ID NO: 21.

In a preferred aspect, *amyB* comprises a nucleotide sequence having at least 70%, preferably at least 75%, more preferably at least 80%, even more preferably at least 85%, most preferably at least 90%, and even most preferably at least 95% identity to ~~SEQ ID NO: 7~~ SEQ ID NO: 17. In a most preferred aspect, *amyB* comprises the nucleotide sequence of ~~SEQ ID NO: 7~~ SEQ ID NO: 17. In another most preferred aspect, *amyB* consists of the nucleotide sequence of ~~SEQ ID NO: 7~~ SEQ ID NO: 17.

In another preferred aspect, *amyB* comprises a nucleotide sequence which hybridizes under very low stringency conditions, preferably low stringency conditions, more preferably medium stringency conditions, more preferably medium-high stringency conditions, even more preferably high stringency conditions, and most preferably very high stringency conditions with ~~SEQ ID NO: 7~~ SEQ ID NO: 17.

In a preferred aspect, *oah* comprises a nucleotide sequence having at least 70%, preferably at least 75%, more preferably at least 80%, even more preferably at least 85%, most

preferably at least 90%, and even most preferably at least 95% identity to ~~SEQ ID NO: 9~~ SEQ ID NO: 23. In a most preferred aspect, *oah* comprises the nucleotide sequence of ~~SEQ ID NO: 9~~ SEQ ID NO: 23. In another most preferred aspect, *oah* consists of the nucleotide sequence of ~~SEQ ID NO: 9~~ SEQ ID NO: 23.

In another preferred aspect, *oah* comprises a nucleotide sequence which hybridizes under very low stringency conditions, preferably low stringency conditions, more preferably medium stringency conditions, more preferably medium-high stringency conditions, even more preferably high stringency conditions, and most preferably very high stringency conditions with ~~SEQ ID NO: 9~~ SEQ ID NO: 23.

In a preferred aspect, *prtT* comprises a nucleotide sequence having at least 70%, preferably at least 75%, more preferably at least 80%, even more preferably at least 85%, most preferably at least 90%, and even most preferably at least 95% identity to ~~SEQ ID NO: 11~~ SEQ ID NO:13. In a most preferred aspect, *prtT* comprises the nucleotide sequence of ~~SEQ ID NO: 11~~ SEQ ID NO:13. In another most preferred aspect, *prtT* consists of the nucleotide sequence of ~~SEQ ID NO: 11~~ SEQ ID NO:13.

In another preferred aspect, *prtT* comprises a nucleotide sequence which hybridizes under very low stringency conditions, preferably low stringency conditions, more preferably medium stringency conditions, more preferably medium-high stringency conditions, even more preferably high stringency conditions, and most preferably very high stringency conditions with ~~SEQ ID NO: 11~~ SEQ ID NO:13.

For purposes of the present invention, the degree of identity between two nucleotide sequences is determined by the Wilbur-Lipman method (Wilbur and Lipman, 1983, *Proceedings of the National Academy of Science USA* 80: 726-730) using the LASERGENE™ MEGALIGN™ software (DNASTAR, Inc., Madison, WI) with an identity table and the following multiple alignment parameters: Gap penalty of 10 and gap length penalty of 10. Pairwise alignment parameters are Ktuple=3, gap penalty=3, and windows=20.

The nucleotide sequences disclosed herein or a subsequence thereof, as well as the amino acid sequence thereof or a fragment thereof, may be used to design a nucleic acid probe to identify and clone DNA encoding enzymes involved in the biosynthesis of hyaluronic acid from strains of different genera or species according to methods well known in the art. In particular, such probes can be used for hybridization with the genomic or cDNA of the genus or species of interest, following standard Southern blotting procedures, in order to identify and isolate the corresponding gene therein. Such probes can be considerably shorter than the entire sequence, but should be at least 15, preferably at least 25, and more preferably at least 35 nucleotides in length. Longer probes can also be used. Both DNA and RNA probes can be used. The probes are typically labeled for detecting the corresponding gene (for example, with